Letter to the Editor

A Red Herring in the Detection of Bence-Jones protein

In about 20% of patients with myelomatosis there is no circulating paraprotein, and the demonstration of Bence-Jones proteinuria becomes a crucial part of the diagnostic process (Hobbs, 1971). The following case illustrates the importance of using adequate technical methods.

A woman aged 55, who had been on steroids for asthma for many years, presented with a two-year history of back pain, and pathological fractures of the femur and two thoracic vertebrae. There was radiological evidence of focal osteolytic bone disease and of generalized osteoporosis. She had proteinuria, and was thought to have multiple myelomatosis possibly with renal amyloidosis.

The total plasma protein concentration was 5·6 g/100 ml and albumin 3·0 g/100 ml. Electrophoresis of the plasma proteins showed no evidence of a paraprotein band. The γ-globulin was decreased, and the immunoglobulin concentrations were IgG 450 mg/100 ml, IgA 121 mg/100 ml, and IgM 70 mg/100 ml. A bone marrow biopsy showed no abnormality of the plasma cells or lymphocytes.

A concentrated dark-brown early-morning urine specimen contained protein. The heat test for Bence-Jones protein (Jones, 1847) was carried out at *p*H 4·9 under the conditions of ionic strength recommended by Putnam, Easley, Lynn, Ritchie, and Phelps (1959). A moderate precipitate had appeared after heating at 56° for 15 minutes, indicating the presence of Bence-Jones protein. When the urine was boiled the density of the precipitate increased, but no precipitate reappeared when the hot filtrate was allowed to cool. The stained urine protein electrophoresis strip showed a generalized proteinuria, together with a sharp 'paraprotein' band in the slow α_2 position.

Since a normal bone marrow biopsy does not exclude the presence of myelomatosis, the evidence at this stage was thought to indicate that the patient had a dedifferentiated myeloma producing only light polypeptide chains, and that the protein behaved in an anomalous fashion in the heat test. However, no paraprotein could be detected when the urine was examined by immunoelectrophoresis. Antisera to κ and λ-light polypeptide chains showed the presence of normal immunoglobulins only. When the electrophoretic separation of the urinary proteins on cellulose acetate membrane was examined before staining, the 'paraprotein' band was seen to be a faint reddish-brown, and staining with a peroxidase stain, *o*-tolidine/hydrogen peroxide, showed that this was a haem protein.

The patient died of a pulmonary embolism shortly after these investigations were completed, and postmortem examination (Dr D. G. F. Harriman) showed numerous deposits of a reticulum cell sarcoma.

The many variations of the heat test for Bence-Jones protein are unsatisfactory as screening procedures because of a failure rate of up to 33% (Hobbs, 1966). False positives may be given by a high concentration of α_1-globulins, or, as shown here, by haemoglobin. The insolubility of haemoglobin at 57° at *p*H 5·28 is, in fact, the basis of a method for separating it from carboxyhaemoglobin (Whitehead and Worthington, 1961). The most sensitive methods for the detection of Bence-Jones proteinuria are electrophoresis of the concentrated urine followed by immunoelectrophoresis (Hobbs, 1966).

It is important to bear in mind that mild haemoglobinuria can both give a positive heat test and appear as a 'paraprotein' band on simple electrophoresis.

I am grateful to Professor B. E. C. Nordin for permission to publish the case report of this patient who was under his care.

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Book reviews

The Circulating Platelet Edited by Shirley A. Johnson. (Pp. xvii + 601; illustrated. $29.50.) New York, London: Academic Press. 1971.

Platelets are a hot topic these days and many monographs and symposia have recently been devoted to them. Of the three new volumes on the subject which have arrived on my desk during the last month, the present expensive production has perhaps the most enticing title. But do not be misled: the emphasis on *in-vivo* observations which it implies is hardly borne out by the contents, which consist of 16 review articles by distinguished research workers on different aspects of platelet structure and function, most of them largely based on the results on *in-vitro* experiments. Although ostensibly intended for a wider readership, this is really a book for platelet specialists: they will be pleased to possess it as a fitting memorial to Dr Shirley Johnson, whose untimely death is widely regretted. The book cannot be recommended to those without much previous knowledge of the subject, who will find it difficult to appraise many of the chapters—several of which are highly controversial.

R. M. HARDISTY

Blood Disorders in the Elderly By J. H. Thomas and D. E. B. Powell. (Pp. v + 284; 85 figures; 29 tables. £4·50.) Bristol; John Wright and Sons Ltd. 1971.

The authors of this book disclaim any intention of writing a textbook of haematology and state their aim as bridging the gap between geriatrics and haematology. However, the types of blood disorder found in older people differ very little from those seen in more general haematological practice and the chapter headings in this book cover the whole range of the subject. If a textbook of haematology were truncated so as to exclude references to subjects below the

age of 60 the result might be less useful than the entire text. In the opening account given here of the prevalence of anaemia figures are given for older age groups even when the papers referred to deal with a much wider age range and therefore give a wider perspective to the problem.

Geriatricians seeking advice on haematological problems might have been better served by a more dogmatic approach. While the chapter on iron deficiency mentions all the tests in common use there is no clear statement of diagnostic criteria. It would be useful to know that the MCHC can remain normal even in the presence of marked deficiency and that in the day of the Coulter S the MCV is a very useful index. The impression is given that a low transferrin saturation is a specific indication of iron deficiency—it can, of course, also occur in chronic infections. Similarly no specific aid is given to those wishing to differentiate a benign from a malignant paraproteinaemia. This volume may serve to make geriatricians more aware of blood diseases in their patients but for detailed information they will have to look to other sources.

A. JACOBS

Recent Advances in Haematology Edited by A. Goldberg and M. C. Brain (Pp. vi + 387; illustrated. £4·00.) Edinburgh and London: Churchill Livingstone. 1971.

This book consists of 10 chapters under the authorship of eminent specialists in their fields. They deal respectively with 'Megaloblastic anaemias' (A. V. Hoffbrand), 'Disorders of iron metabolism' (J. H. Dagg, R. L. C. Cummings, and A. Goldberg), 'The red cell and haemolytic anaemia (M. C. Brain), 'Abnormal haemoglobins' (D. J. Weatherall), 'Treatment of malignant blood diseases' (G. Hamilton Fairley), 'Platelets, haemostasis and thrombosis (A. G. G. Turpie, G. P. McNicol, and A. S. Douglas), 'Porphyrins and porphyrias' (A. Goldberg), 'Anaemia in the tropics (W. R. Pitney), 'Automation in haematology' (B. S. Bull), and 'Leucocyte groups in blood and their relation to transplantation antigens' (J. J. van Rood).

This is the twenty-sixth in the *Recent Advances* series. Previously, haematology had been included as a brief section in *Recent Advances in Clinical Pathology*, but now haematology warrants its own named series. Some of the authors of this first volume have taken the title of the book seriously and have described at greater or lesser length only recent advances in their field; others, eg, Hoffbrand and Dagg, Cummings, and Goldberg have interpreted rather more widely and have contributed 70-80-page reviews. Their references to the literature have been extensive and comprehensive, but where there have been different opinions expressed in various published reports it would have been of even greater value if there had been more selectivity on the basis of the personal authority and experience of the writers. Weatherall, in a relatively short chapter (with only 70 references), provides a fascinating insight into current concepts of the molecular pathology of haemoglobin disorders. Hamilton Fairley has given a brief outline of the commonly available forms of treatment for various malignant blood diseases, and has shown how, over the past 10 years, both the form of therapy and the approach to the patient have changed; his own extensive experience provides valuable information. Pitney's chapter on anaemia in the tropics describes disorders which are also included in other chapters, eg, iron-deficiency anaemia and megaloblastic anaemias. The particular value of this chapter is in describing the implications of these diseases in terms of public health and socio-economic problems. Brain has written on the advances which have taken place over the past few years in studies of red cell structure and function and haemolytic anaemias; he has, in a clear style and in the span of 33 pages, described the interrelationship of membrane structure and function, metabolism, and haemoglobin constitution, all of which influence the prime function of the cell in the transport and delivery of oxygen. One of the shortest chapters, a mere 10 pages, is that on automation. This subject is of increasing importance but in this review it is dismissed with scant reference to the considerable bibliography which has appeared in recent years, and with little or no reference to the question of standardization, quality control, and the principles of instrumentation, all of which would have been valuable material in this context.

The selection of topics will obviously not satisfy everybody and there are other aspects of haematology, equally important, and on which there has been considerable developments in recent years, which have not been included. It is strange, for example, to find no reference to leucopoiesis and leucocyte kinetics, whereas two-thirds of the book is devoted to erythropoiesis and the red blood cell; however, the advantage of a series of this nature is that these deficiencies can be compensated in the next edition. Without doubt, this present edition deserves and is assured of an enthusiastic reception from haematologists. Its immediate purpose is to update the standard textbooks and in general it can be said to have done so with great success; it provides an enormous amount of factual material and a sufficient bibliography to keep the zealot looking up the sources of these references for many a month to come.

S. M. LEWIS

Notices

Enzyme Assays in Medicine

The proceedings of the symposium on 'Enzyme assays in medicine' organized by the Association of Clinical Pathologists is published as a supplement to the *Journal of Clinical Pathology*, price £2·00 including postage. Members of the Association of Clinical Pathologists receive this automatically, but members of the Royal College of Pathologists and subscribers to the *Journal of Clinical Pathology* can buy the supplement at the concessionary price of £1·75, including postage. Copies may be obtained from the Publishing Manager, BMA House, Tavistock Square, London WC1H 9JR.

SI Units

From 1972 all measurements in chemical pathology and haematology in the Journal, where appropriate, should be expressed in SI units (*J. clin. Path.*, 23, 818-819). Most papers which have already been accepted will retain the original nomenclature, but would authors submitting new papers kindly use SI units with the old notation following in brackets.